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Portacaval Shunt in Patients with Cirrhosis

After-Effects of the Operation

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• **The subject of the indications for operation for portacaval shunt bristles with problems to which a satisfactory answer cannot yet be given. I have discussed those events which supervene after a portacaval shunt which, in the present state of knowledge, has been directed as proper and well-intentioned therapy. It is against the knowledge of such post-shunt events and the complexity of their management, as well as the success of the operation and the risk of mortality, that one must balance the indications for surgery. This is particularly pertinent to the application of prophylactic shunt surgery now under consideration.**

BEFORE DISCUSSING some of the empirical results in patients with chronic liver disease upon whom such shunting operation has been performed, I would like to enumerate some of the physiologic events which can be expected. If one creates in dogs a side-to-side anastomosis between the portal vein and the inferior vena cava below the liver (Figure 1A), the only impaired function which can be measured is that of regeneration of liver tissue after partial hepatectomy. If one then ligates the portal vein on the liver's side of the portacaval anastomosis (Figure 1B), thereby creating an Eck fistula, further changes ensue. (Such an Eck fistula is duplicated in humans, incidentally, by a standard end-to-side anastomosis (Figure 1C) between the portal vein and the inferior vena cava.) Animals that have had these operations undergo gradual atrophy of the liver. After some delay a progressive episodic stuporous condition, which has been called "meat intoxication," begins. This occurs whether or not meat is present in the diet and seems to be more clearly related to constipating diets. Protection of such dogs from the "meat intoxication" of an Eck fistula can be afforded by gradual occlusion of the portal vein below the fistula (Figure 1D). Complete recovery from the symptoms of Eck fistula is also effected if the vena cava above the portacaval anastomosis is occluded (Figure 1E). Bollman[2] speculated that the common denominator here is prevention of pulse waves from the right heart down through the anastomosis and portal system to the intestines.

Portacaval anastomosis halves the blood flow through the liver of animals.[3] Perhaps because the terminal parenchyma along the vascular system is quite hypoxic, tests of liver function show impairment after portacaval anastomosis. For example, the by-passed liver can then clear only one-third as much bromsulphalein each minute as the liver of a normal animal can. Furthermore, there is a decreased output of glucose by the liver after stimulation with insulin. Whipple,[14] using Eck fistula preparations, found that production of bile salts was

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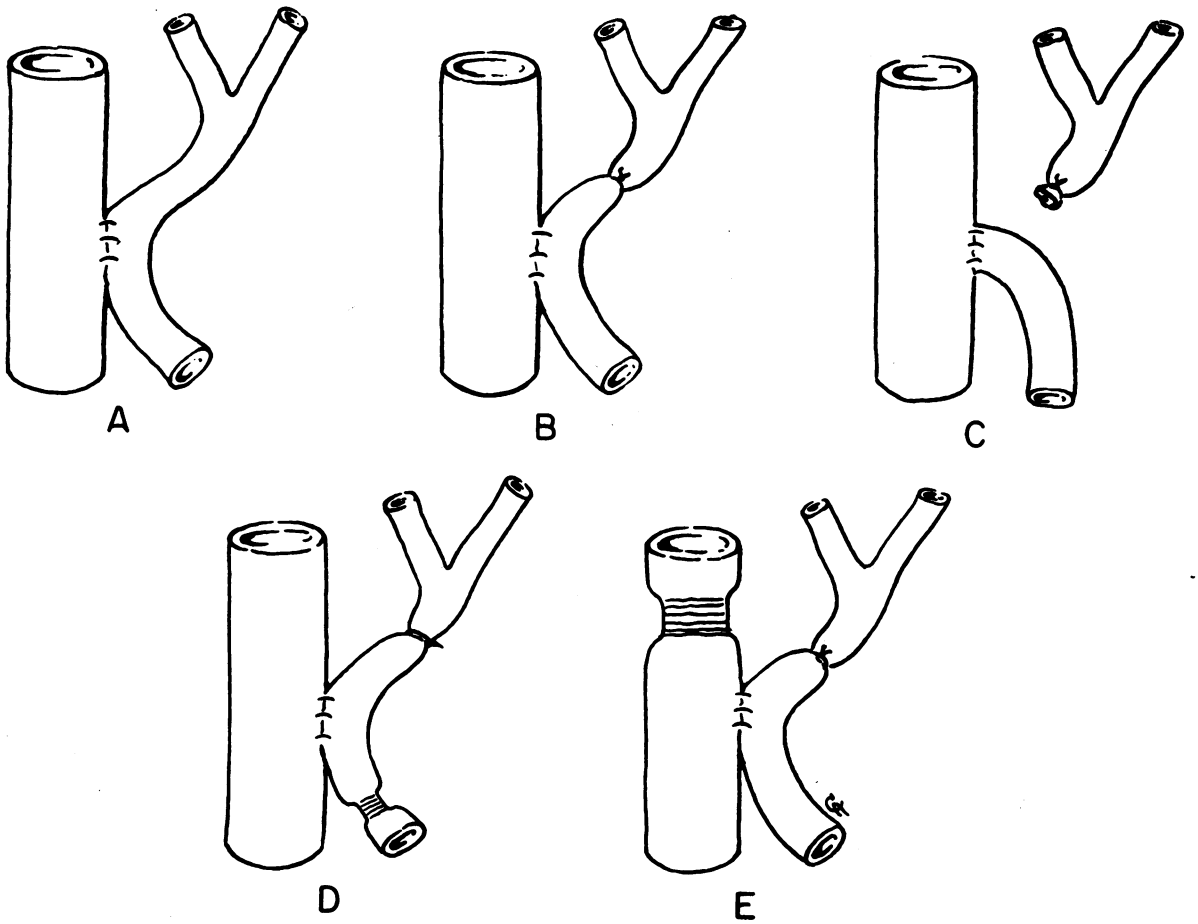

Figure 1.—Various placements for portacaval anastomosis, the inferior vena cava just below the liver always appearing on the left: *A.* Side-to-side portacaval shunt. *B.* Side-to-side portacaval shunt with ligation of portal vein above the shunt, or an Eck fistula. *C.* End-to-side portacaval shunt. *D.* Eck fistula with occlusion of portal vein below the shunt by cellophane stricture. *E.* Eck fistula with occlusion of the inferior vena cava above the shunt by cellophane stricture.

less than normal. There also were periods of a definite incapacity to utilize dietary protein in the formation of new hemoglobin and plasma proteins, and the utilization of ingested iron toward correction of a nutritional anemia was less efficient.

In dogs the ability of the remaining normal liver to regenerate after partial hepatectomy or injury by carbon tetrachloride is impaired by a portacaval anastomosis. Repair after partial hepatectomy is better if portacaval transposition is performed instead. Such a transposition perfuses the liver through the portal vein with caval blood from the kidneys and lower extremities. Liver regeneration is also improved by arterialization of the hepatic stub of the portal vein in an animal with an end-to-side portacaval shunt.[8] Such animals with total arterialization of the liver maintain body weight, have a greater survival and do not develop "meat intoxication," in contrast to those with Eck fistula. Thus it would seem that the ability of the liver to regenerate depends in part on adequate flow of blood through it.

The condition referred to as "meat intoxication" deserves further comment. In dogs, such episodic stuporous states have been observed with non-specific changes in electroencephalograms and eventually elevations of the blood ammonia. The episodes of intoxication occur at an accelerating pace, despite the administration of oxytetracycline or neomycin by mouth and irrespective of a limited oral intake of protein, until the animals die in 12 weeks or so, emaciated and comatose. Their brains show increased numbers of protoplasmic astrocytes.

DIFFERENCES IN EXPERIENCE IN HUMANS

In considering the relationship of the foregoing facts to corresponding conditions in human beings, it must be borne in mind that in humans we are dealing not with a normal liver or hepatic circulation, but with one affected by chronic disease. End-to-side portacaval shunt in a human with cirrhosis of the liver is not regularly attended by either episodic stupor or relentless deterioration to early

death. This difference deserves emphasis. There are at least two possible reasons why a human with cirrhosis does better than a dog with an Eck fistula. First, the dog that has also had an occlusion of the portal vein (Figure 1D) with development of adequate collaterals, is protected from "meat intoxication" and death. A corollary of this exists in the human who before a shunting operation has acquired spontaneous collaterals. Second, the regenerated nodule of the cirrhotic liver is perfused, not by the portal vein, but by branches of the hepatic artery. Therefore, sudden diversion of portal venous blood through a surgical shunt does not suddenly deprive regenerated liver of its principal blood supply.

The main effects of the portacaval anastomosis are, to my mind, beneficial. In this field there have been no universally acceptable, controlled series that clearly delineate the value, or worthlessness, of venous shunts in the reduction of bleeding from esophageal varices. Because it seems that a reasonably safe and feasible operation might reduce the horrible toll of such bleeding in some patients, and because we cannot comfortably deprive patients of this hope, portacaval shunts will probably continue to be done without proper statistical validation.

SURVIVAL

The overall mortality rate of elective shunting operations in the hands of interested and expert surgeons is now around 10 to 15 per cent. Statistically, if a group of patients with cirrhosis, in whom varices are diagnosed before bleeding begins, were observed for only two years, 80 per cent might be expected to die in that time. Although many of the deaths would not be caused directly by exsanguination, at least 10 to 15 per cent of patients having cirrhosis and varices may be expected to die eventually from their first hemorrhage.[1] About 75 per cent of patients with esophageal varices that have bled once may be expected to die within one year of the first hemorrhage, a figure which has not changed in the past 20 years. Bleeding therefore greatly lessens the predicted survival. On the other hand, of a series of patients at Massachusetts General Hospital who had a shunting procedure because of esophageal bleeding, only about one-third died within two years.[6] The mortality rate associated with splenorenal shunts was lower than with portacaval shunts, perhaps because of the greater incidence of postoperative liver failure after the latter procedure. The first year or two is the most critical period. Patients with varices known to have been present for at least two years without bleeding have a relatively good survival rate and the same is true of those who live for over two years after a shunting operation. The longer the patient survives, the less important liver disease becomes as a cause of death. In one series only about 12 per cent died of hepatic failure.

BLEEDING AFTER SHUNT OPERATIONS

There should be no further gastrointestinal bleeding after a shunting operation. In Child's series,[5] hemorrhage recurred only when the portal venous pressure had not been adequately reduced. Nevertheless, various series show recurrent bleeding in 14 to 31.5 per cent of cases. It is generally conceded to be more common after splenorenal than after portacaval shunts. Linton[6] reported esophageal bleeding in 17 per cent of patients with splenorenal shunts and in only 3 per cent of patients with portacaval anastomosis, although only 2 per cent died of bleeding. Recurring bleeding is not necessarily a sign of portal hypertension or of closure of the anastomosis. Abdominal wall collateral veins should disappear along with any venous hums which might have been present. Esophageal varices, as visualized by barium swallow, generally disappear in patients with satisfactory decrease in portal pressure. The disappearance may take from three to six months. Their presence does not necessarily signify portal hypertension, but if the x-ray films show residual varices beyond six months after operation, the effectiveness of the operation may be questioned.

LIVER FUNCTION

Even in persons without liver disease, laboratory tests of liver function become mildly abnormal after such minor operations as herniorrhaphy or vein stripping and somewhat more abnormal after major upper abdominal operations such as gastrectomy. If the patient has cirrhosis, this immediate deterioration in results of standard tests of liver function is more severe. The changes include a fall in serum albumin and rises in serum bilirubin, alkaline phosphatase and bromsulphalein retention. Usually within ten to fourteen days the values have reverted to preoperative levels. In patients with chronic liver disease there is apparently no greater deterioration after portacaval shunt than after operations of comparable severity in the upper abdomen. The changes in liver function tests are probably related more to the preoperative state of liver function than to the operation itself. In patients who survive the operation there is no significant worsening in results of tests of liver function over the ensuing five years. The test values, moreover, have not been helpful in predicting the well-being of the patient. Indeed, many a patient who feels vastly better after operation has distressingly abnormal results of liver function tests.

EFFECTS OF SPLENECTOMY

The relief of portal hypertension by portacaval shunt is usually attended by decrease in size of the spleen. However, there is no consistent improvement in the granulocytopenia or thrombocytopenia that is associated with congestion of the spleen. There are isolated examples of improvement in hypersplenism, even when the spleen has been left in after a portacaval shunt. But the majority of investigators agree with MacPherson[7] that such improvment is unusual without splenectomy. MacPherson noted evidence of improved resistance to repeated respiratory tract infections in three such patients following the addition of splenectomy. The splenorenal shunt is, of course, preferred by some observers because of the splenectomy which it entails, removing both the splenic arterial inflow into the portal system and the short gastric veins which feed into esophageal varices. Splenectomy has been attended by only a 7 per cent incidence of thrombosis extending into the splenic and portal veins, an incidence no higher than that in persons with hepatic cirrhosis who are not operated on. Splenectomy does not usually alleviate the Coombs negative reduction in erythrocyte survival observed in some persons with cirrhosis of the liver.

CHANGES IN PORTAL PRESSURE

Usually when thrombosis closes the lumen at the site of anastomosis, the event occurs in the immediate postoperative period. The complication is commoner after splenorenal anastomosis and side-to-side portacaval shunt. If this occurs, or if the shunt has not been effective in reducing the portal venous pressure below 30 cm. of water or so, the operation may be considered a failure, whatever happens to the patient. But usually this pressure is not accurately known. It may be determined, if desired, by recording the splenic pulp pressure percutaneously in patients who have had portacaval shunt or the wedged hepatic venous pressure in cirrhotic patients who have had splenectomy.

Before a surgical shunt is created, the portal venous pressure is highest in persons in whom the greatest number of spontaneously induced collaterals have formed. Therefore the latter are not effective ordinarily in decompressing the portal hypertension. Furthermore, the portal venous pressure is higher in patients with varices that bleed than in those with varices that have not bled. So it seems desirable to reduce portal venous pressure. Following portacaval shunt, Rousselot[11] obtained an average fall of 22 cm. of water to a final pressure of 22 cm. The decrease after splenorenal anastomosis was somewhat less, the average reduction having been 15 cm. of water to a final pressure of 24 cm. Reynolds[10] observed a fall in both the portal venous pressure and in the wedged hepatic venous pressure. Sherlock[12] reported a decrease in the splenic pulp pressure. But the pressures were not reduced to normal, and therefore the hepatic vascular resistance at the postsinusoidal level was maintained.

FALL IN LIVER BLOOD FLOW

There is also a fall in the estimated hepatic blood flow after venous shunt operations. After splenorenal shunt, this decrease is of the order of 25 per cent, whereas after portacaval anastomosis it is about 40 per cent.[10,12] This amounts to a reduction of around 700 ml. per minute in flow of blood after portacaval shunts. While this represents a respectable decrease in blood flow, it must be recognized that after the operation the hepatic artery is carrying a greatly increased proportion of the total blood flow, especially to the regenerated liver tissue. Despite the decrease in hepatic blood flow, there is no measurable fall in oxygen consumption by the liver.[4] This is accomplished by a greater extraction of oxygen from a given volume of blood. The hepatic venous oxygen content after shunts, for example, is usually less than 10 volumes per cent. One might presume from such information that the parenchyma supplied by the distal end of the hepatic circulation might suffer from hypoxia, but such a presumption is belied by the fact that bromsulphalein extraction is well maintained and usually there is no progressive worsening in liver function as a result of the shunt.

FLUID RETENTION

If the patient had had ascites before operation, it tends to recur briefly in the immediate postoperative period. Edema at the ankle on dependence of the extremity sometimes develops or increases after portacaval shunt. This is not necessarily accompanied by an increase in the pressure in the inferior vena cava, and it is seldom much of a clinical problem. These evidences of fluid retention are curious, for an increasing number of patients are being subjected to portacaval shunts for the relief of ascites. In cases in which the operation for this purpose succeeds, a change in the ratio of urinary sodium to potassium occurs consistent with relief of a hyperaldosterone effect—that is, more sodium and less potassium is excreted.[9]

BEHAVIOR AND STUPOR

A problem in the behavior of a neuropsychiatric nature occurs in some 15 to 20 per cent of patients after portacaval shunt.[13] Von Eck described "meat intoxication" in dogs late in the last century, and the problem and even the mechanism have been observed in men for hundreds of years. In 1602

Shakespeare alluded to this in *Twelfth Night:* Sir Toby Belch says to his friend, Sir Andrew Aguecheek: "Oh, Knight! Thou lackest a cup of canary; when did I see thee so put down?" And Sir Andrew answers: "Never in your life, I think; unless you see canary put me down. Methinks sometimes I have no more wit than a Christian or an ordinary man has; but I am a great eater of beef, and I believe that does harm to my wit."

There is no sure way of predicting the incidence of such encephalopathic states. Surely a patient who has had it preoperatively may be more liable to it after a shunt is performed. Unfortunately the various predictive tests applied have given uncertain correlation. These include symptoms from ingestion of methionine, a prolonged elevation of venous blood ammonia after oral ammonium administration, and intolerance to diets containing 120 gm. or more of protein per day. Apparently behavior problems of this order follow portacaval shunt far more commonly than they do splenorenal shunt.

The usual onset of these symptoms is several weeks to months following the creation of the shunt. At first the patients may not notice that they are drowsier and occasionally confused. There is a simple disorganization of thinking with poor retentiveness and poor cooperation with complex requests. The family may appreciate this earlier than the patient, but the patient generally realizes that something is amiss. Later there is a slowing of physical movements and the development of a non-intention, flapping tremor when activating the muscles of the outstretched, extended fingers, lips or head. This flapping tremor is not specific to chronic liver disease, for it also occurs in uremia and respiratory alkalosis. The tremor, interestingly, is not seen in patients or animals with an Eck fistula. As the condition progresses, there may be twitching or even convulsions with variable deep tendon reflexes, inconstant extensor plantar responses, hypertonicity of the muscles, rousable stupor, the specific fetor and, finally, deep coma. Unless other central nervous system disease is present there are no persistent lateralizing neurological signs.

The subtle, early changes may be unmasked by certain discriminative tests. The patient may be asked to write an unfamiliar phrase each day in his record, which may divulge deterioration in his handwriting. With giggling futility, he may find himself completely unable to copy the examiner's example of a five-pointed star constructed from wooden matches. Unless he has long been familiar with mathematics, he is likely to stumble badly at subtracting seven serially from 100. The electroencephalogram is probably the most sensitive means of quantitating the problem. During the confused stage, 5 to 6 per second waves of about 50 microvolts appear, spreading from original sites in the frontal areas. As stupor deepens, the voltage increases and the rate of this diffuse delta activity slows to 2 to 3 per second. In deep coma, triphasic waves may appear. Such reversible patterns have also been noticed in vitamin B_{12} deficiency, hypokalemia and hypoglycemia, but not in experimental Eck fistula.

Various precipitating factors have been demonstrated. Tolerance to barbiturates and opiates is notoriously poor in persons with hepatic cirrhosis. Eight milligrams of morphine can slow the electroencephalographic waves in persons with a tendency toward coma without altering the blood pH or the potassium or ammonia content, according to Sherlock.[13] Effective diuretic programs may also produce electroencephalographic changes and clinical precoma by leading to huge potassium deficits. Progressive encephalomalacia from arteriosclerosis renders the older patients more susceptible. Hypoglycemia is poorly tolerated. These factors are not influenced by protein restriction or by administration of neomycin.

Whenever excessive nitrogen reaches the increased bacterial flora of the small intestine in persons with cirrhosis, whether it is due to dietary protein or gastrointestinal bleeding, this neuropsychiatric syndrome may result. Oral administration of ammonium chloride, methionine and cation exchange resins which swap ammonium for sodium and potassium may also initiate such deterioration. Precoma sometimes follows use of amine-oxidase inhibitors, but most investigators, finding no elevation in blood amines, doubt that the latter contribute to this state.

Among 21 candidates with portacaval shunt and chronic liver disease, Sherlock[13] noted eight with episodic stupor, four with abnormal electroencephalograms, three whose EEGs were labile to oral ammonium chloride, and only six with normal tracings. Perhaps some sensitization of the brain is necessary before patients react. Such factors probably include preexisting cerebral disease, ammonia, unconjugated bilirubin, serotonin deficiency, disordered carbohydrate metabolism, anoxemia, narcotics, infection and hypokalemic alkalosis.

The treatment of porta-systemic encephalopathic states after portacaval shunt is usually at least partially successful. Dietary protein should be limited to what the patient can tolerate; 30 to 40 gm. a day ordinarily maintains a positive nitrogen balance. Precipitating factors must be eliminated. Intestinal antiseptics such as neomycin, 4 gm. daily, usually suppress offending coliform flora. Potassium, carbohydrate and vitamin B_{12} deficits must be replaced. Hemodialysis, glutamic acid, arginine, and dilantin are generally worthless.

Finally, what is the capacity of these patients to carry on after operation? In the Massachusetts General Hospital series,[6] 82 survivors were observed for periods of from one to ten years. Two thirds of them were doing well, unaware of physical limitations and able to undertake full work or household duties. One fourth were reasonably active but handicapped by some physical limitation, half of the time due to progressive cirrhosis. Only 7 per cent remained incapacitated by cirrhosis. Many, despite exhaustive preoperative medical treatment, seemed to be much better postoperatively than before. These changes included an improved feeling of well-being and strength, restoration of normal skin color, return of normal fullness of the face, weight gain, restoration of normal musculature, and regrowth of previously sparse axillary and pubic hair. Venous shunt operations may lead to improvement in organ systems such as the small intestine as well as in the liver itself.

While this improvement occurs at a high price on the contemporary medical market, the drawbacks which have been outlined should not deter physicians from offering portacaval shunt as proper and judicious therapy.

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